4 days resulted in suppression of testosterone to castrate levels, accompanied by an increase in the oral bioavailability of AG-045572 to 27%. In the same experiment, the male-specific pulsatile pattern of growth hormone remained unchanged, with slightly elevated basal levels. The potent GnRH receptor antagonist AG-045572 is metabolized by hormone-dependent CYP3A. As a result, suppression of testosterone by pretreatment with AG-045572 "feminized" its own pharmacokinetics.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:241135 CAPLUS
DOCUMENT NUMBER: 132:279106
TITLE: Non-peptide GnRH agents, methods and intermediates for their preparation
INVENTOR(S): Anderson, Mark Brian; Vazir, Haresh N.; Luthin, David Robert; Paderes, Genevieve Deguzman; Pathak, Ved P.; Christie, Lance Christopher; Hong, Yufeng; Tompkins, Eileen Valenzuela; Li, Haitao; Faust, James
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA; et al.
SOURCE: PCT Int. Appl., 444 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000020358 | A2 | 20000413 | WO 1999-US18790 | 19990820 |
| WO 2000020358 | A3 | 20001116 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2341346 | A1 | 20000413 | CA 1999-2341346 | 19990820 |
| BR 9913374 | A | 20010515 | BR 1999-13374 | 19990820 |
| EP 1105120 | A2 | 20010613 | EP 1999-968010 | 19990820 |
| EP 1105120 | B1 | 20050323 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |

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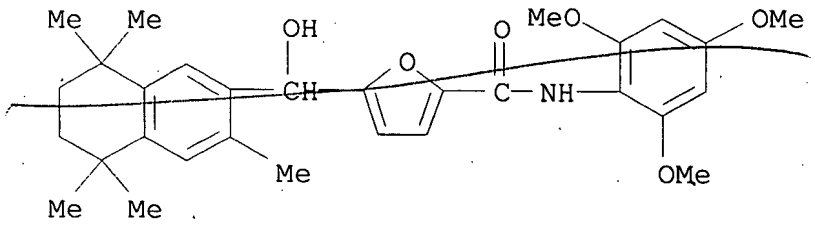
|---|---|---|---|---|---|
| HU 200103622 | A2 | 20020429 | HU 2001-3622 | | 19990820 |
| EE 200100102 | A | 20020617 | EE 2001-102 | | 19990820 |
| SI 20746 | A | 20020630 | SI 1999-20076 | | 19990820 |
| TR 200100631 | T2 | 20020821 | TR 2001-200100631 | | 19990820 |
| JP 2002535244 | T | 20021022 | JP 2000-574479 | | 19990820 |
| AU 759310 | B2 | 20030410 | AU 2000-24709 | | 19990820 |
| NZ 509252 | A | 20040528 | NZ 1999-509252 | | 19990820 |
| AT 291423 | T | 20050415 | AT 1999-968010 | | 19990820 |
| ES 2237966 | T3 | 20050801 | ES 1999-968010 | | 19990820 |
| NO 2001000309 | A | 20010411 | NO 2001-309 | | 20010119 |
| IN 2001DN00066 | A | 20070112 | IN 2001-DN66 | | 20010124 |
| ZA 2001000831 | A | 20020822 | ZA 2001-831 | | 20010130 |
| MX 2001PA01834 | A | 20000821 | MX 2001-PA1834 | | 20010219 |
| US 7101878 | B1 | 20060905 | US 2001-763216 | | 20010220 |
| LV 12732 | B | 20020320 | LV 2001-45 | | 20010316 |
| BG 105362 | A | 20011231 | BG 2001-105362 | | 20010319 |
| LT 4904 | B | 20020425 | LT 2001-24 | | 20010319 |
| US 2004010033 | A1 | 20040115 | US 2003-353160 | | 20030708 |
| PRIORITY APPLN. INFO.: | | | US 1998-97520P | P | 19980820 |
| | | | WO 1999-US18790 | W | 19990820 |
| | | | US 2001-763216 | B3 | 20010220 |

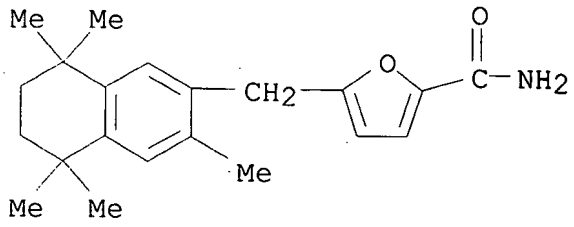
OTHER SOURCE(S): MARPAT 132:279106

IT 263850-02-8P 263850-03-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(comparison compound; preparation of non-peptide GnRH agents for regulating gonadotropin secretion)

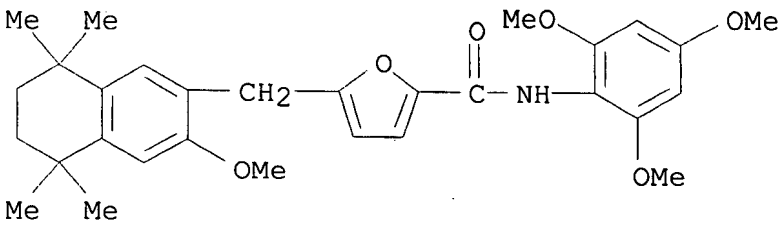
RN 263850-02-8 CAPLUS
CN 2-Furancarboxamide, 5-[hydroxy(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-N-(2,4,6-trimethoxyphenyl)- (9CI) (CA INDEX NAME)



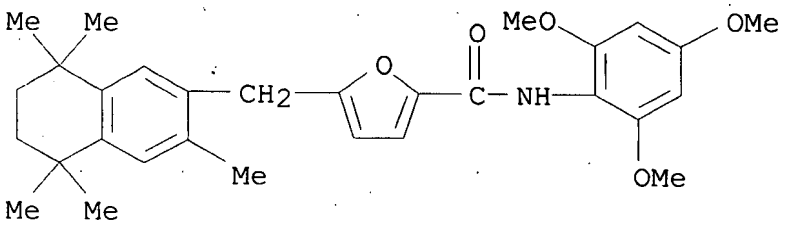

RN 263850-03-9 CAPLUS
CN 2-Furancarboxamide, 5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



IT 263878-35-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of non-peptide GnRH agents for regulating gonadotropin secretion)
RN 263878-35-9 CAPLUS
CN 2-Furancarboxamide, 5-[(5,6,7,8-tetrahydro-3-methoxy-5,5,8,8-tetramethyl-2-naphthalenyl)methyl]-N-(2,4,6-trimethoxyphenyl)- (9CI) (CA INDEX NAME)

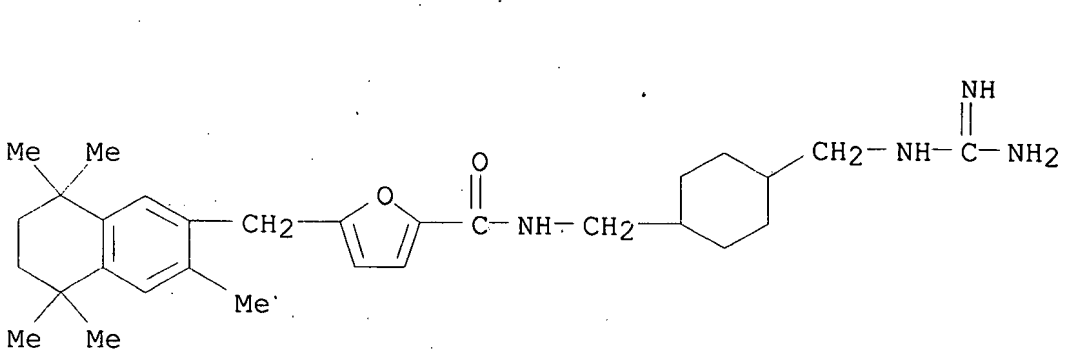


IT 263848-89-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of non-peptide GnRH agents for regulating gonadotropin secretion)
RN 263848-89-1 CAPLUS
CN 2-Furancarboxamide, N-[[3-(aminomethyl)phenyl]methyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



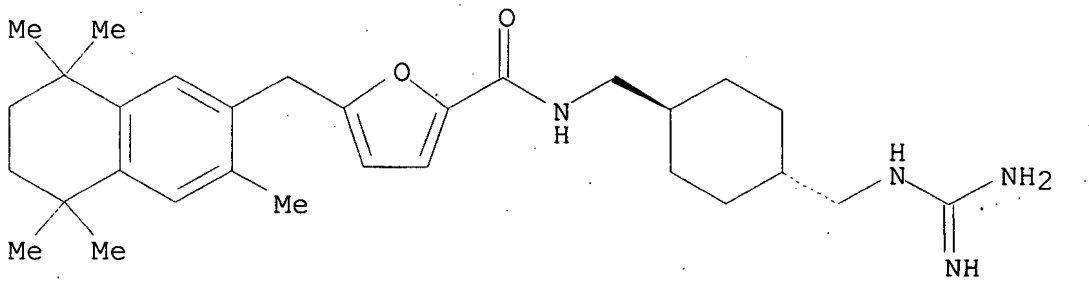
RN 263847-61-6 CAPLUS
CN 2-Furancarboxamide,
N-[[4-[[(aminoiminomethyl)amino]methyl]cyclohexyl]meth

yl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-
(9CI) (CA INDEX NAME)

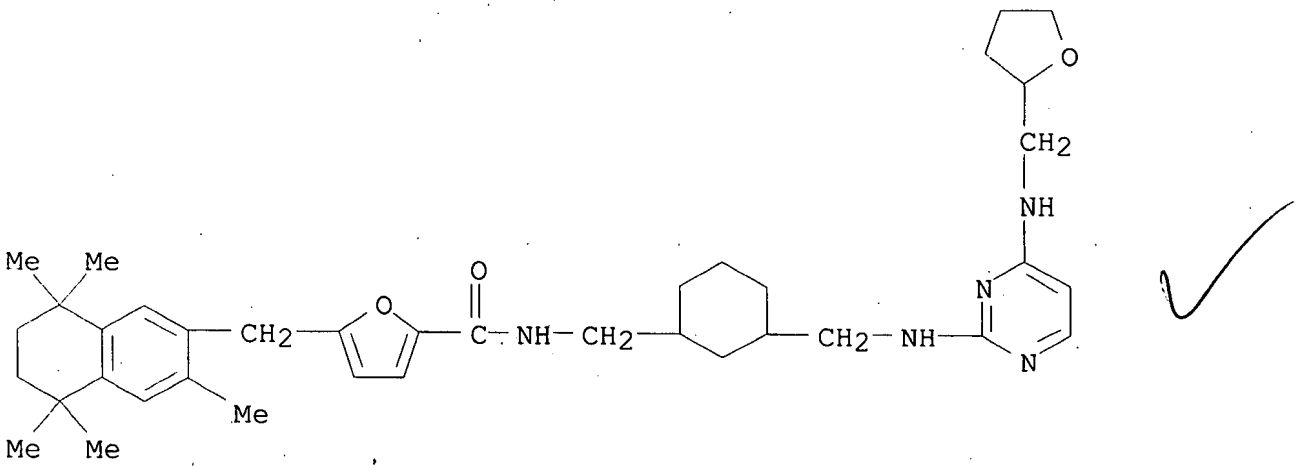


RN 263847-62-7 CAPLUS
CN 2-Furancarboxamide,
N-[[trans-4-[[(aminoiminomethyl)amino]methyl]cyclohexy
l]methyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-
naphthalenyl)methyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

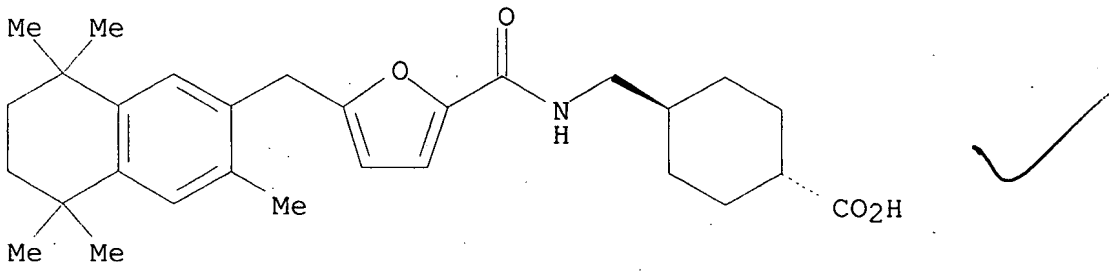


RN 263847-63-8 CAPLUS
CN 2-Furancarboxamide, N-[[3-[[[4-[[(tetrahydro-2-furanyl)methyl]amino]-2-
pyrimidinyl]amino]methyl]cyclohexyl]methyl]-5-[(5,6,7,8-tetrahydro-
3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)

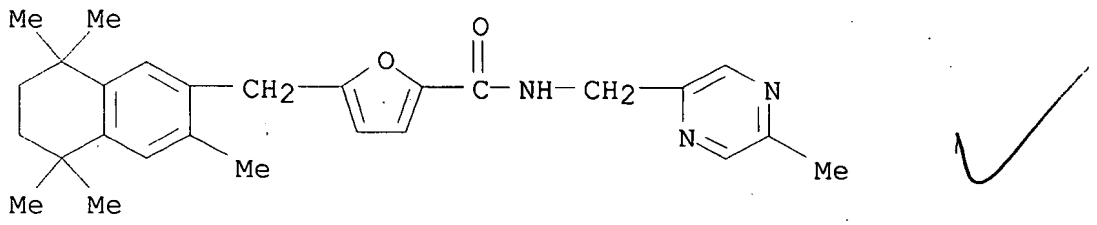


RN 263847-64-9 CAPLUS
CN Cyclohexanecarboxylic acid, 4-[[[[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-2-furanyl]carbonyl]amino]methyl]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

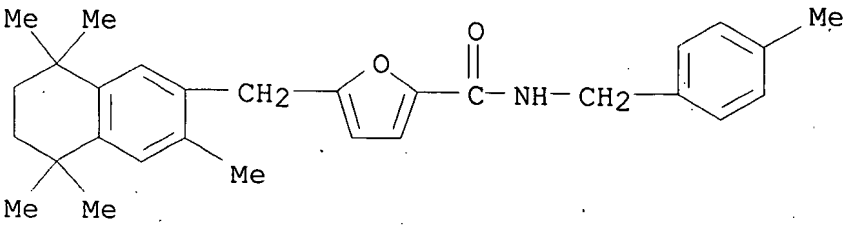


RN 263847-65-0 CAPLUS
CN 2-Furancarboxamide, N-[(5-methylpyrazinyl)methyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)

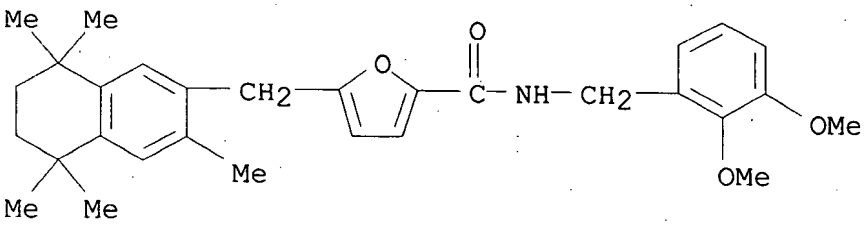


RN 263847-66-1 CAPLUS

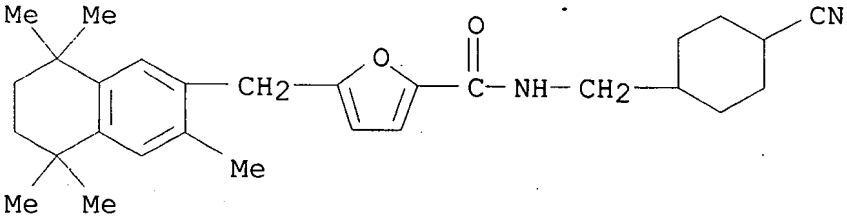
CN 2-Furancarboxamide, N-[(4-methylphenyl)methyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (CA INDEX NAME)



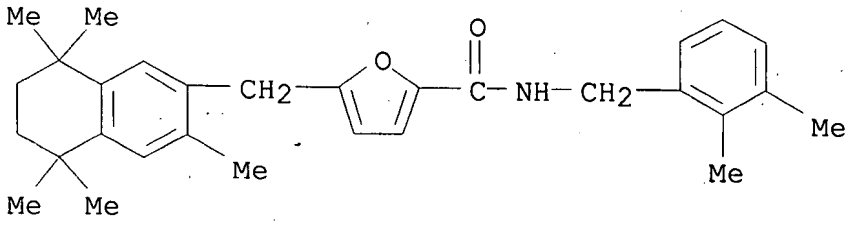
RN 263847-67-2 CAPLUS
CN 2-Furancarboxamide,
N-[(2,3-dimethoxyphenyl)methyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



RN 263847-68-3 CAPLUS
CN 2-Furancarboxamide,
N-[(4-cyanocyclohexyl)methyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



RN 263847-69-4 CAPLUS
CN 2-Furancarboxamide,
N-[(2,3-dimethylphenyl)methyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



RN 263847-70-7 CAPLUS
CN 2-Furancarboxamide,
N-[(3,4-dimethylphenyl)methyl]-5-[(5,6,7,8-tetrahydro-
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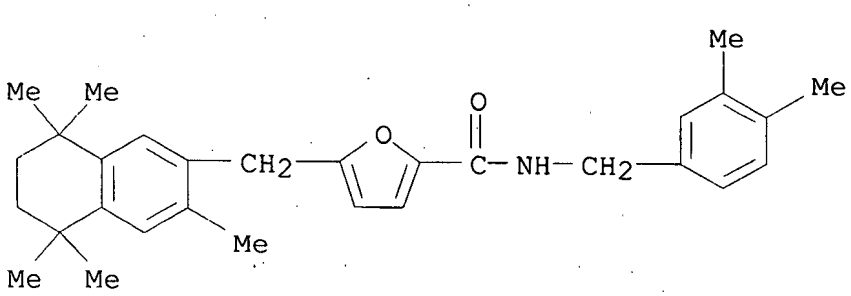
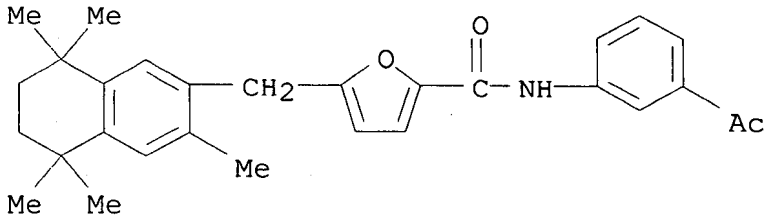
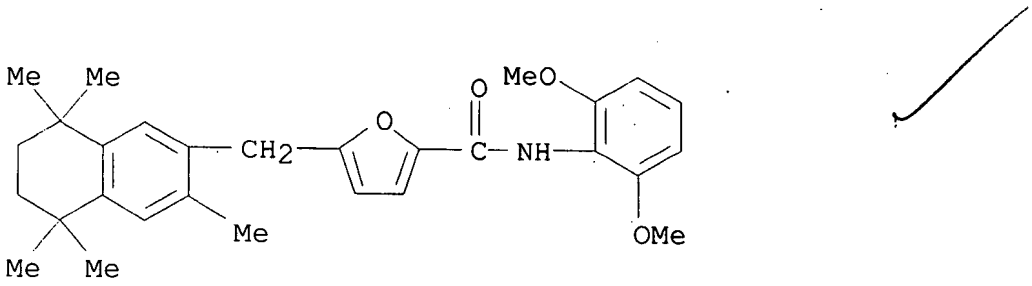


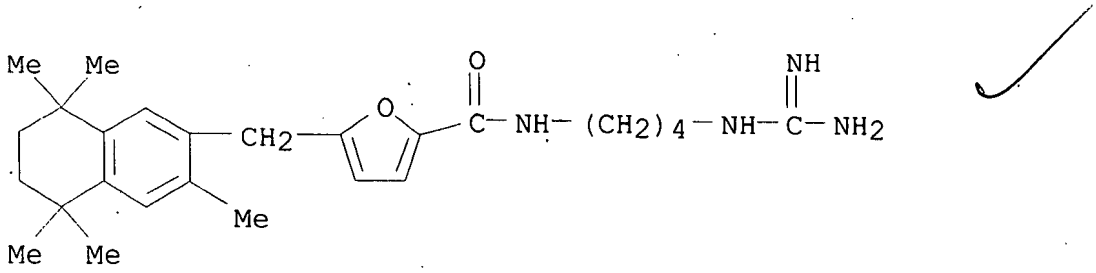
RN 263847-71-8 CAPLUS
CN 2-Furancarboxamide,
N-(3-acetylphenyl)-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-
pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



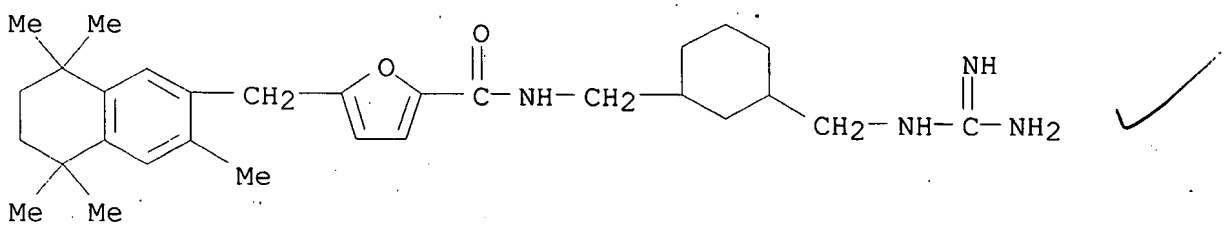
RN 263847-72-9 CAPLUS
CN 2-Furancarboxamide, N-(2,6-dimethoxyphenyl)-5-[(5,6,7,8-tetrahydro-
3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



RN 263847-73-0 CAPLUS
CN 2-Furancarboxamide, N-[4-[(aminoiminomethyl)amino]butyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)

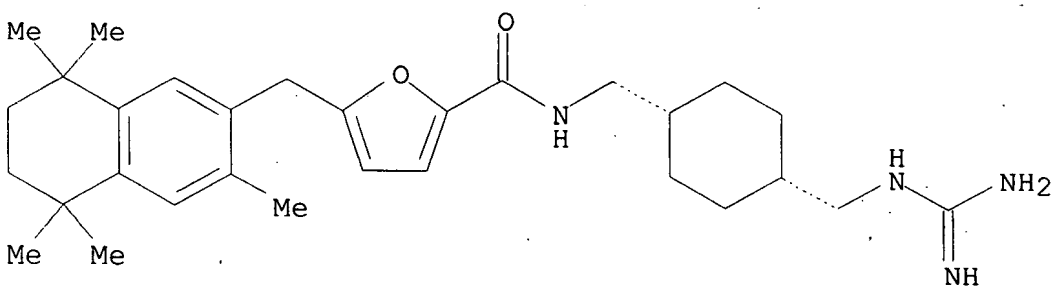


RN 263847-74-1 CAPLUS
CN 2-Furancarboxamide, N-[[3-[[(aminoiminomethyl)amino]methyl]cyclohexyl]methyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)

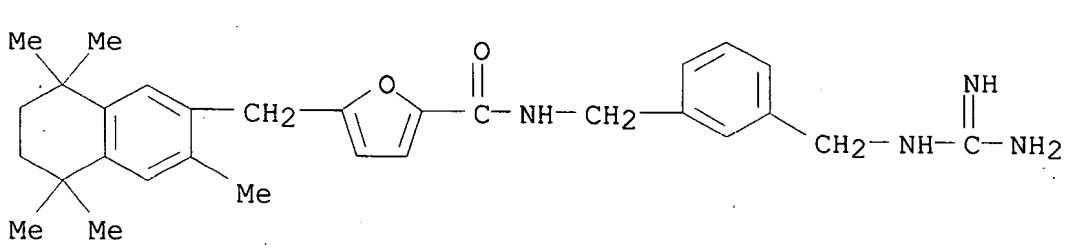


RN 263847-75-2 CAPLUS
CN 2-Furancarboxamide, N-[[cis-4-[[(aminoiminomethyl)amino]methyl]cyclohexyl]methyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)

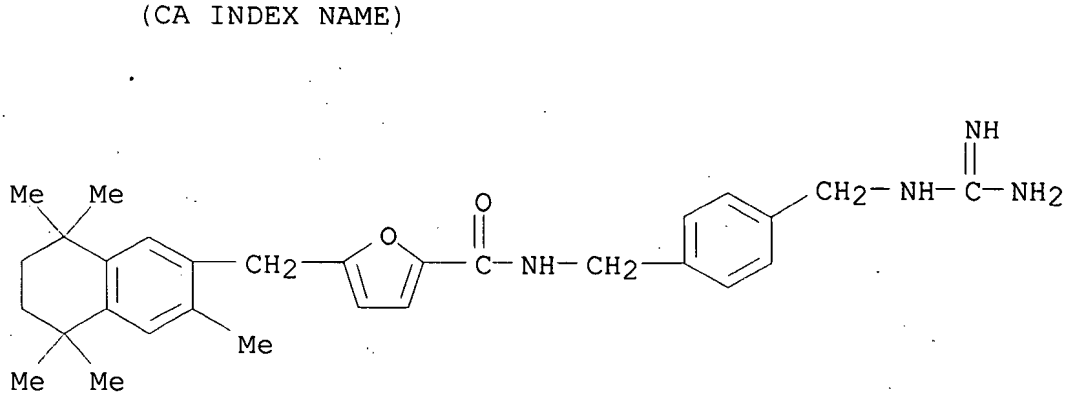
Relative stereochemistry.



RN 263847-76-3 CAPLUS
CN 2-Furancarboxamide,
N-[[3-[[(aminoiminomethyl)amino]methyl]phenyl]methyl]-
5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-
(9CI)
(CA INDEX NAME)

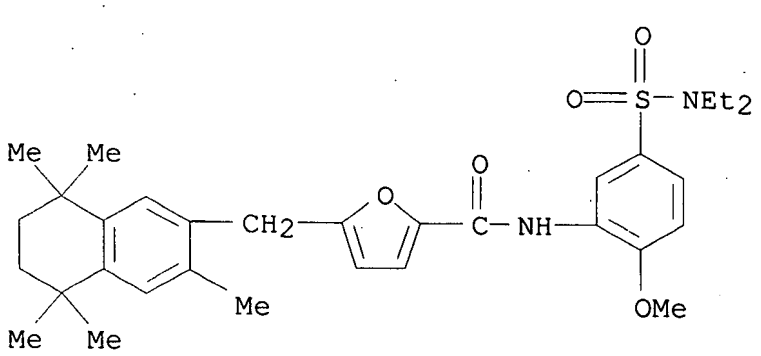


RN 263847-77-4 CAPLUS
CN 2-Furancarboxamide,
N-[[4-[[(aminoiminomethyl)amino]methyl]phenyl]methyl]-
5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-
(9CI)
(CA INDEX NAME)



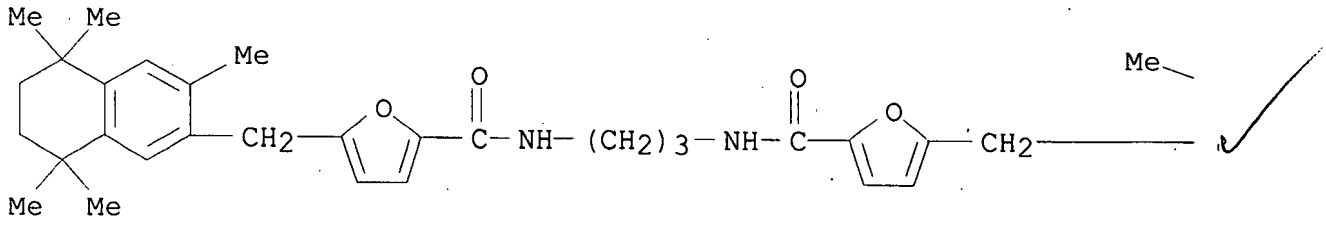
RN 263847-78-5 CAPLUS
CN 2-Furancarboxamide, N-[5-[(diethylamino)sulfonyl]-2-methoxyphenyl]-5-
[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-
(9CI)

(CA INDEX NAME)

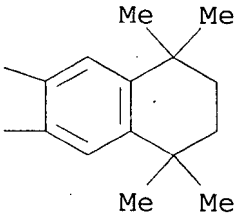


RN 263847-79-6 CAPLUS
CN 2-Furancarboxamide, N,N'-1,3-propanediylbis[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

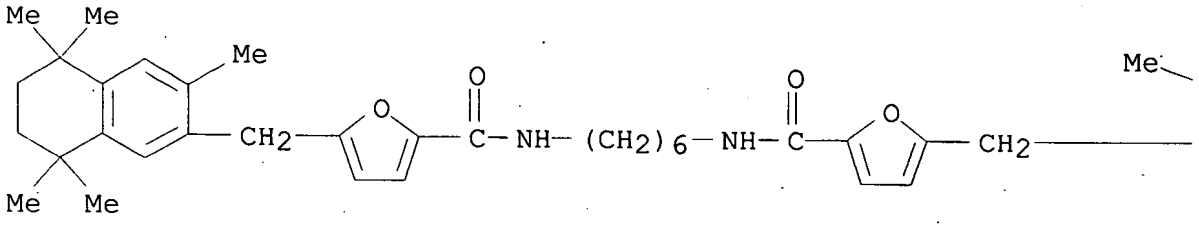


PAGE 1-B



RN 263847-80-9 CAPLUS
CN 2-Furancarboxamide, N,N'-1,6-hexanediylbis[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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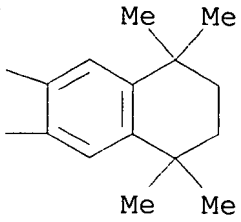
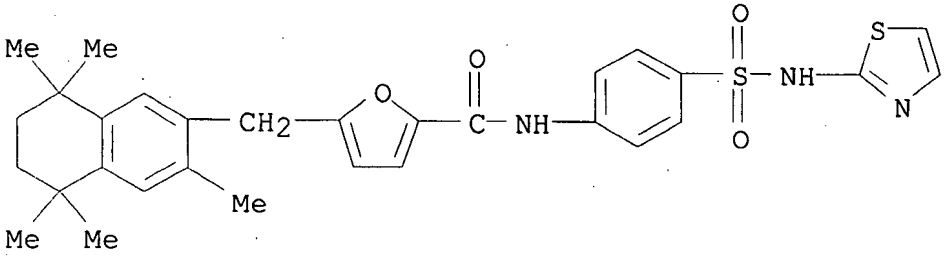
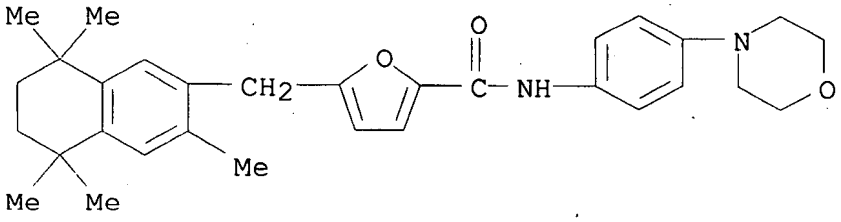


RN 263847-81-0 CAPLUS
CN 2-Furancarboxamide, 5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-N-[4-[(2-thiazolylamino)sulfonyl]phenyl]- (9CI) (CA INDEX NAME)

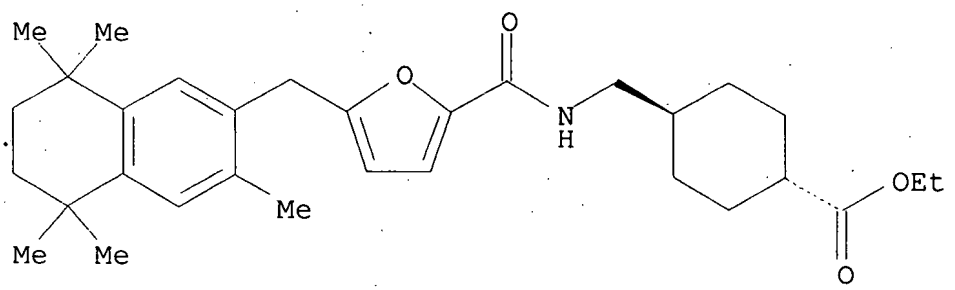


RN 263847-82-1 CAPLUS
CN 2-Furancarboxamide, N-[4-(4-morpholinyl)phenyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)

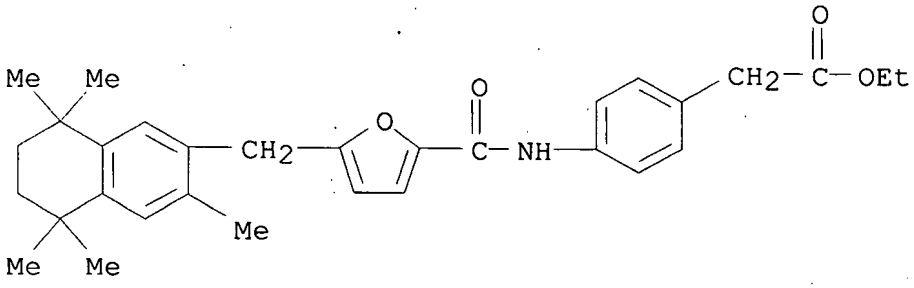


RN 263847-83-2 CAPLUS
CN Cyclohexanecarboxylic acid, 4-[[[[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-2-furanyl]carbonyl]amino]methyl]-, ethyl ester, trans- (9CI) (CA INDEX NAME)

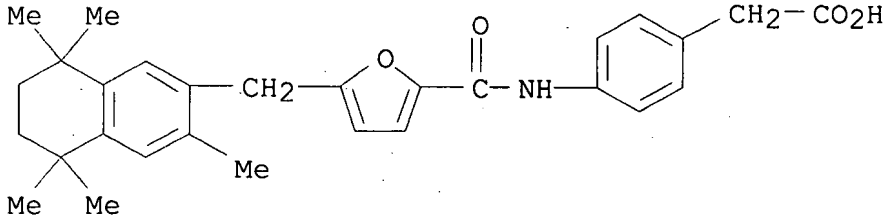
Relative stereochemistry.



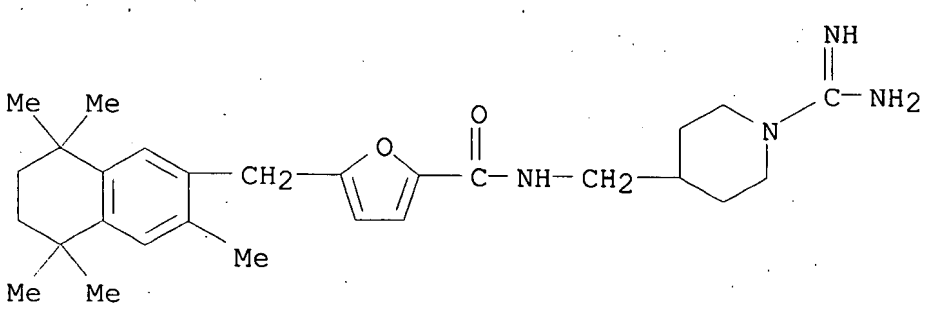
RN 263847-84-3 CAPLUS
CN Benzeneacetic acid, 4-[[[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-2-furanyl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



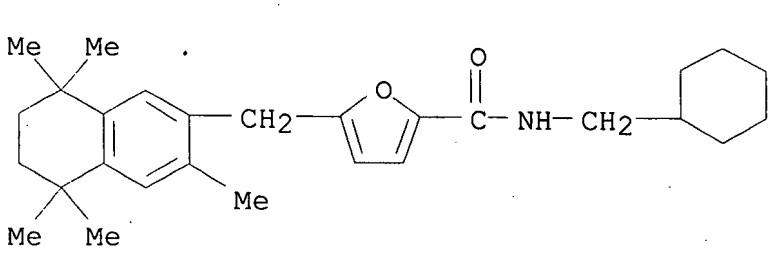
RN 263847-85-4 CAPLUS
CN Benzeneacetic acid, 4-[[[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-2-furanyl]carbonyl]amino]- (9CI) (CA INDEX NAME)



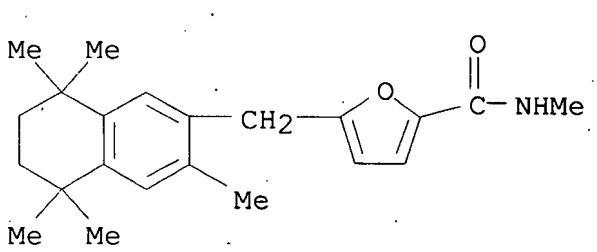
RN 263847-87-6 CAPLUS
CN 2-Furancarboxamide, N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-(9CI)
(CA INDEX NAME)



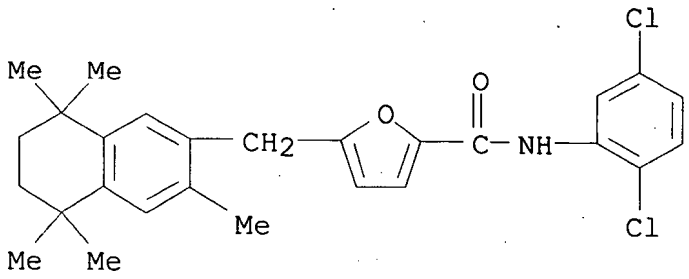
RN 263847-88-7 CAPLUS
CN 2-Furancarboxamide, N-(cyclohexylmethyl)-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



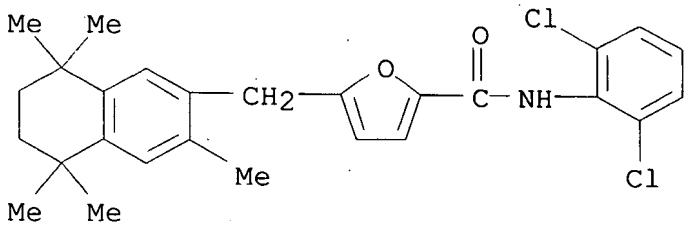
RN 263847-89-8 CAPLUS
CN 2-Furancarboxamide, N-methyl-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



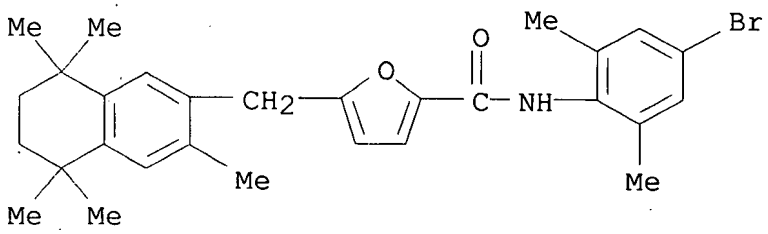
RN 263847-90-1 CAPLUS
CN Hexanoic acid, 6-[[[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-2-furanyl]carbonyl]amino]-, methyl ester (9CI)
(CA



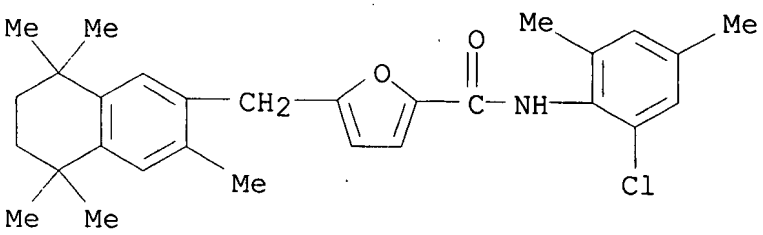
RN 263858-07-7 CAPLUS
CN 2-Furancarboxamide, N-(2,6-dichlorophenyl)-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



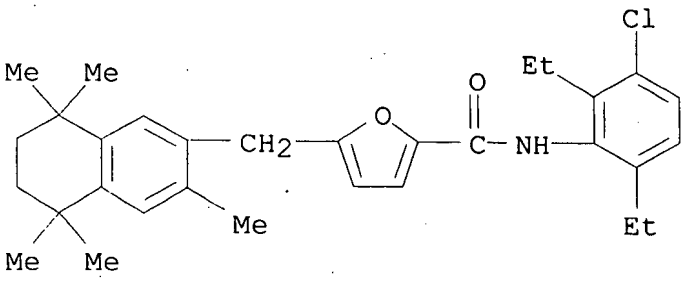
RN 263858-08-8 CAPLUS
CN 2-Furancarboxamide, N-(4-bromo-2,6-dimethylphenyl)-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



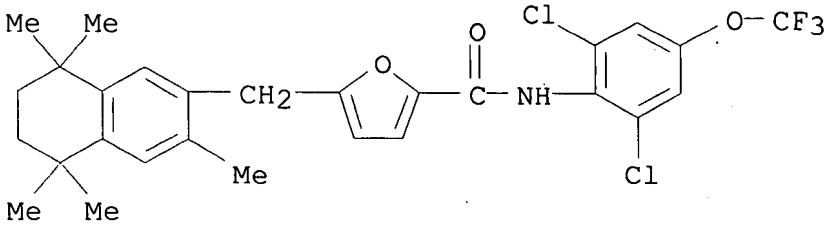
RN 263858-09-9 CAPLUS
CN 2-Furancarboxamide, N-(2-chloro-4,6-dimethylphenyl)-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



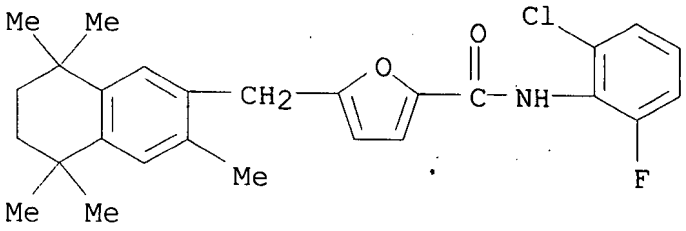
RN 263858-10-2 CAPLUS
CN 2-Furancarboxamide,
N-(3-chloro-2,6-diethylphenyl)-5-[(5,6,7,8-tetrahydro-
3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



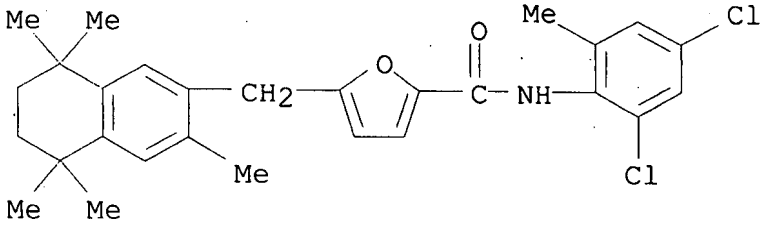
RN 263858-11-3 CAPLUS
CN 2-Furancarboxamide, N-[2,6-dichloro-4-(trifluoromethoxy)phenyl]-5-
[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-
(9CI)
(CA INDEX NAME)



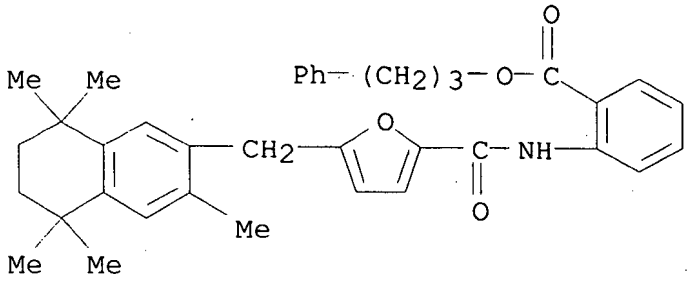
RN 263858-12-4 CAPLUS
CN 2-Furancarboxamide, N-(2-chloro-6-fluorophenyl)-5-[(5,6,7,8-tetrahydro-
3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



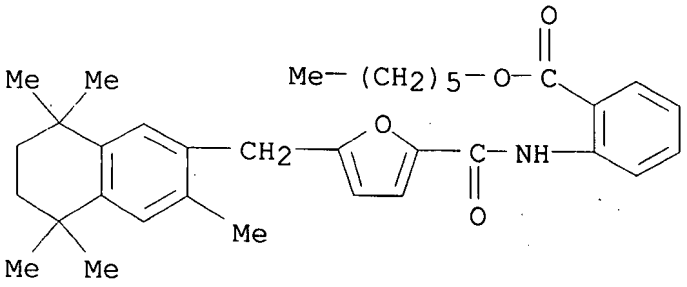
RN 263858-13-5 CAPLUS
CN 2-Furancarboxamide,
N-(2,4-dichloro-6-methylphenyl)-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



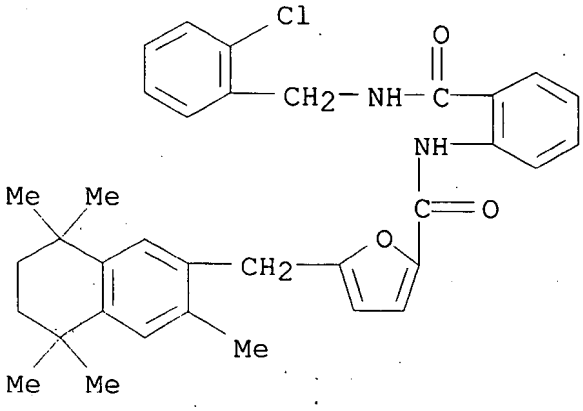
RN 263858-14-6 CAPLUS
CN Benzoic acid, 2-[[[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-2-furanyl]carbonyl]amino]-, 3-phenylpropyl ester (9CI) (CA INDEX NAME)



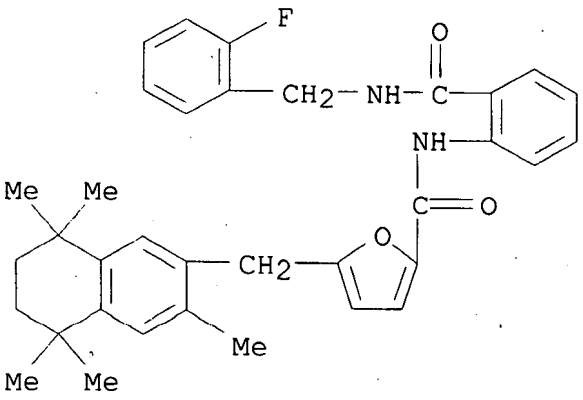
RN 263858-15-7 CAPLUS
CN Benzoic acid, 2-[[[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-2-furanyl]carbonyl]amino]-, hexyl ester (9CI) (CA INDEX NAME)



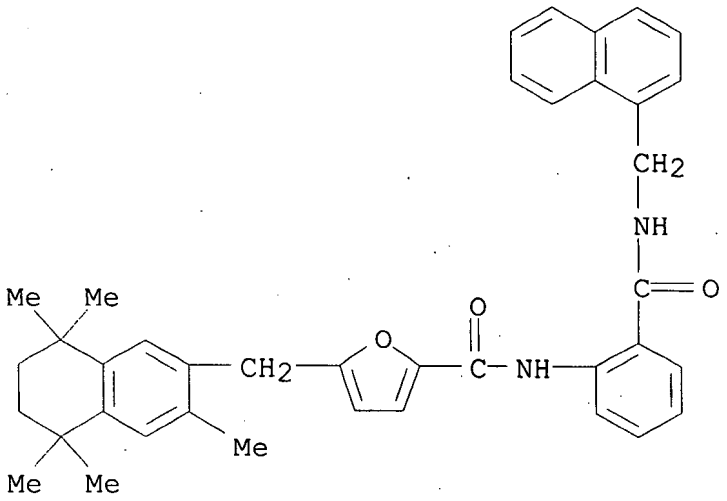
RN 263858-16-8 CAPLUS
CN 2-Furancarboxamide,
N-[2-[[[(2-chlorophenyl)methyl]amino]carbonyl]phenyl]-
5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-
(9CI)
(CA INDEX NAME)



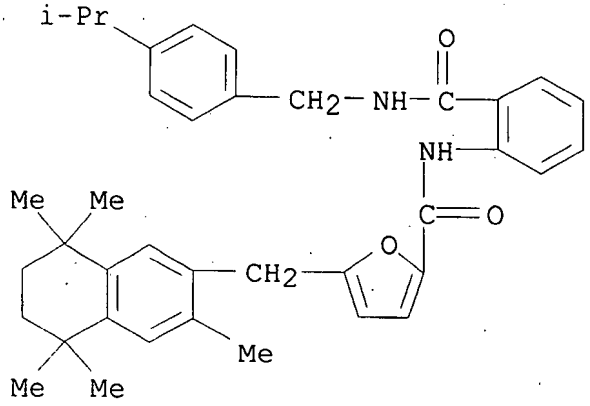
RN 263858-17-9 CAPLUS
CN 2-Furancarboxamide,
N-[2-[[[(2-fluorophenyl)methyl]amino]carbonyl]phenyl]-
5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-
(9CI)
(CA INDEX NAME)



RN 263858-18-0 CAPLUS
CN 2-Furancarboxamide,
N-[2-[[(1-naphthalenylmethyl)amino]carbonyl]phenyl]-5-
[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-
(9CI)
(CA INDEX NAME)

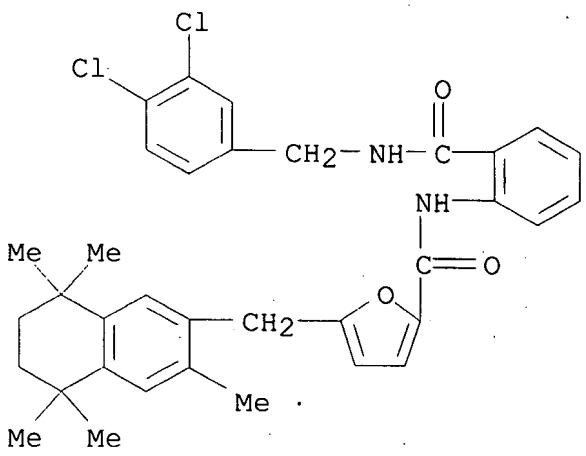


RN 263858-19-1 CAPLUS
CN 2-Furancarboxamide,
N-[2-[[[[4-(1-methylethyl)phenyl]methyl]amino]carbonyl
]phenyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-
naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



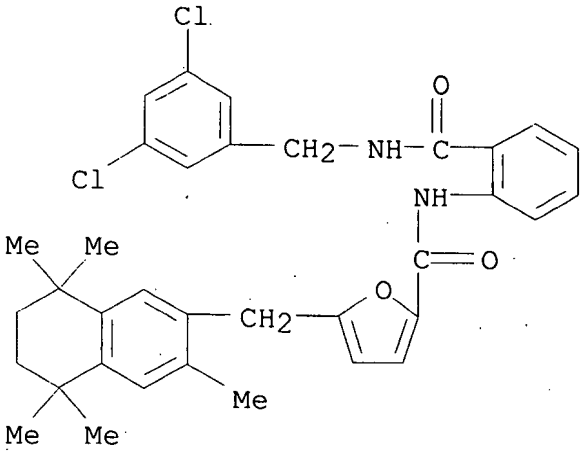
RN 263858-20-4 CAPLUS
CN 2-Furancarboxamide,
N-[2-[[[(3,4-dichlorophenyl)methyl]amino]carbonyl]phen

yl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-
(9CI) (CA INDEX NAME)



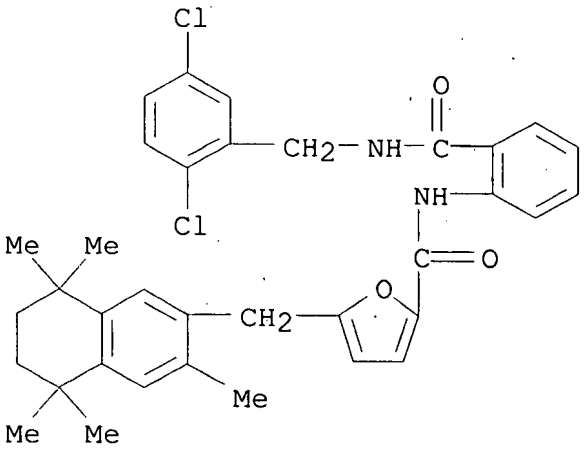
RN 263858-21-5 CAPLUS
CN 2-Furancarboxamide,
N-[2-[[[(3,5-dichlorophenyl)methyl]amino]carbonyl]phen

yl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-
(9CI) (CA INDEX NAME)



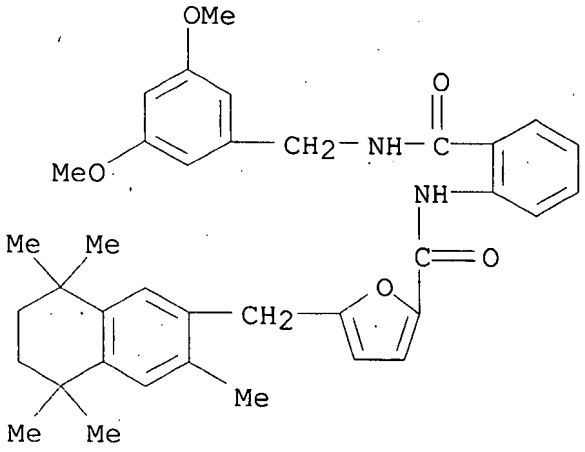
RN 263858-22-6 CAPLUS
CN 2-Furancarboxamide,
N-[2-[[[(2,5-dichlorophenyl)methyl]amino]carbonyl]phen

yl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-
(9CI) (CA INDEX NAME)

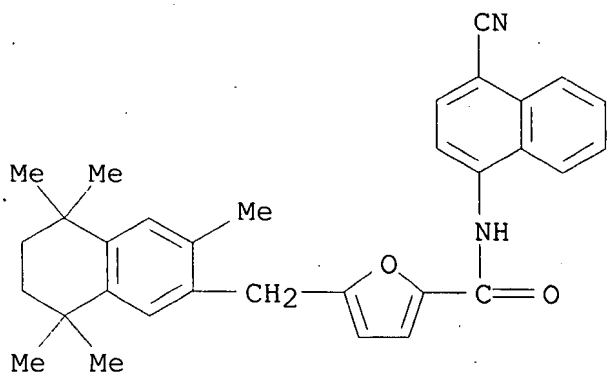


RN 263858-23-7 CAPLUS
CN 2-Furancarboxamide,
N-[2-[[[(3,5-dimethoxyphenyl)methyl]amino]carbonyl]phe

nyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-
(9CI) (CA INDEX NAME)




RN 263858-24-8 CAPLUS
CN 2-Furancarboxamide, N-(4-cyano-1-naphthalenyl)-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)

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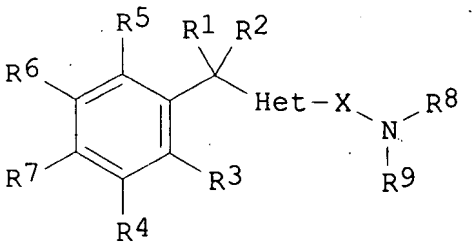


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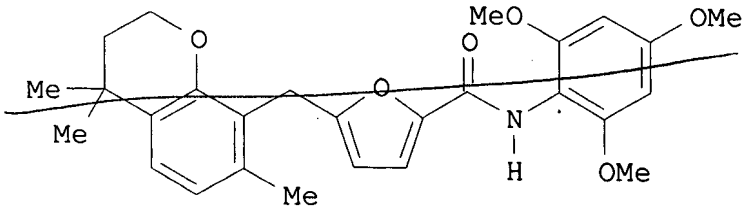


II

AB Non-peptide GnRH agents capable of inhibiting the effect of gonadotropin-releasing hormone are described. The compds. and their pharmaceutically acceptable salts, multimers, prodrugs, and active metabolites are suitable for treating mammalian reproductive disorders and steroid hormone-dependent tumors as well as for regulating fertility, where suppression of gonadotropin release is indicated. The compds. include those of formula I [X = C:O, C:S, S:O, or SO2; Het = 5-membered NOS-heterocycle; R1, R2 = H, alkyl; R3-R7 = H, halo, (un)substituted alkyl, aryl, heteroaryl, CH2OR, OR, CO2R; R = alkyl, aryl, etc.; adjacent rings positions such as R6R7 may form (un)substituted 5- or 6-membered ring with up to 4 heteroatoms; R8 = lipophilic moiety such as alkyl, aryl, CH2OR, OR, etc.; R9 = H, (un)substituted alkyl]. Methods and intermediates for synthesizing the compds. are also described. For instance, 4,4,7-trimethylchroman (preparation given) was alkylated in the 6- and 8-positions using Et 5-(chloromethyl)-2-furoate (46% total yield), and the resulting esters were hydrolyzed to a mixture of acids. This unsepd. mixture was treated with SOCl2 and amidated with 2,4,6-trimethoxyphenylamine-HCl to give the invention compound II and its chroman-6-position isomer, which were separated by HPLC. Several compds. exhibited high affinity (<100 nM) at human GnRH receptors. The compds. antagonized GnRH-stimulated

inositol phosphate accumulation in cells with recombinant human GnRH receptors, and an example compound reduced plasma LH levels in castrated male rats. Various biol. data for several hundred compds. are given.

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| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
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